CARDIOTHORACIC TRANSPLANTATION

HEART TRANSPLANTATION IN INFANTS AND CHILDREN WITH SITUS INVERSUS

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Background: **Recipient situs inversus has always represented a technical challenge during heart transplantation.** ***Objective:*** **A simplified operative strategy for heart transplantation in a recipient with atrial situs inversus is described.** ***Methods:*** **Fifteen pediatric recipients with situs inversus accompanying other complex congenital heart disease or dilated cardiomyopathy having "orthotopic" heart allotransplantation in one center, between 1985 and 1997, were reviewed retrospectively. A nearly uniform, simplified technical approach to transplantation was used and is described.** ***Results:*** **Fourteen of these recipients with complex malformations survived the transplantation. Morbidity relating to surgical technique has been limited to partial ($n = 2$) or complete ($n = 1$) late obstruction of superior vena caval drainage; each case was managed successfully by interventional cardiologic techniques. Actuarial survival after transplantation compares favorably with that among 290 infants and children with atrial situs solitus who underwent heart transplantation.** ***Conclusions:*** **Systemic atrial malposition, including situs inversus, does not limit successful heart transplantation by the simplified method described. (J Thorac Cardiovasc Surg 1998; 116:82-9)**

Orthotopic heart allotransplantation is accomplished in children with complex anatomy that is the result of either multiple prior palliative procedures or de novo congenital cardiac malformations, including atrial malposition. Fifteen patients with atrial situs inversus underwent heart transplantation over a 12-year period. A simplified technique of heart graft implantation in patients with inverted atrial situs or situs ambiguus is presented.

Patients and methods

The database for 15 patients who were diagnosed with atrial situs inversus before the operation, who underwent orthotopic heart allotransplantation between November 1985 and February 1997, was reviewed. These recipients represent 4.9% of the 305 pediatric patients who underwent heart transplantation at Loma Linda University Medical Center and Children's Hospital during the same time period.

Ten girls and five boys with situs inversus were 11 days to 17 years old at the time of transplantation (median, 5.7 ± 5.8 years, standard deviation). Preoperative weight ranged between 2.8 and 96.6 kg (median, 16.8 ± 23.2 kg, standard deviation). Fourteen patients (93%) had complex congenital heart disease, and one patient had end-stage idiopathic cardiomyopathy several years after uneventful repair of a ventricular septal defect. Ten recipients (66%) had previous median sternotomy for a variety of procedures. Six patients (40%) had no spleen; one individual had multiple spleens. Eight recipients (53%) had associated visceral heterotaxia, and three patients (20%)had no spleen and visceral heterotaxia. Immunoregulative strategy was similar for all recipients regardless of the diagnosis of asplenia. Patients with asplenia were placed on a permanent prophylactic antibiotic regimen.

Patient characteristics and other cardiac diagnostic features are summarized in Table I. Median length of posttransplantation follow-up for survivors is 4.2 years (range, 1.0 to 6.3 years).

Operative procedure. The donor-recipient techniques for orthotopic heart transplantation among patients with situs inversus are illustrated in Figs. 1, 2, 3, and 4. The same general simplified approach was used in all patients in this series. Individual modifications were tailored to the patient's coexisting cardiac malformation.

Donor cardiectomy was accomplished with en bloc removal of the superior vena cava (SVC) and innominate

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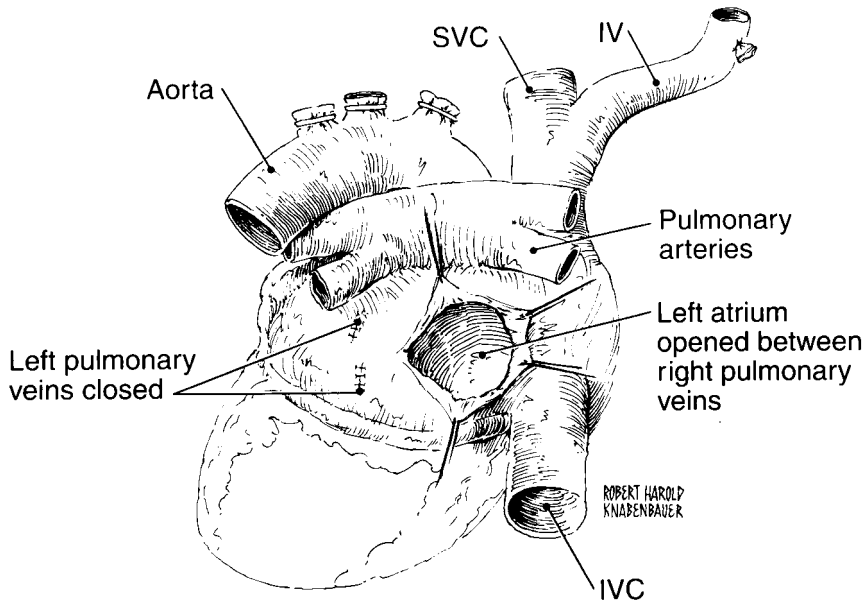

Fig. 1. Appearance of the heart procured from a donor with situs solitus that will be used for transplantation into a recipient with situs inversus. Left pulmonary venous orifices are ligated or oversewn (as depicted here). The left atrium is opened with an incision between the right superior and inferior pulmonary venous orifices and extended transversely as required. Sufficient aortic and pulmonary artery length is obtained to meet specific requirements of the host. *IV*, Donor innominate vein.

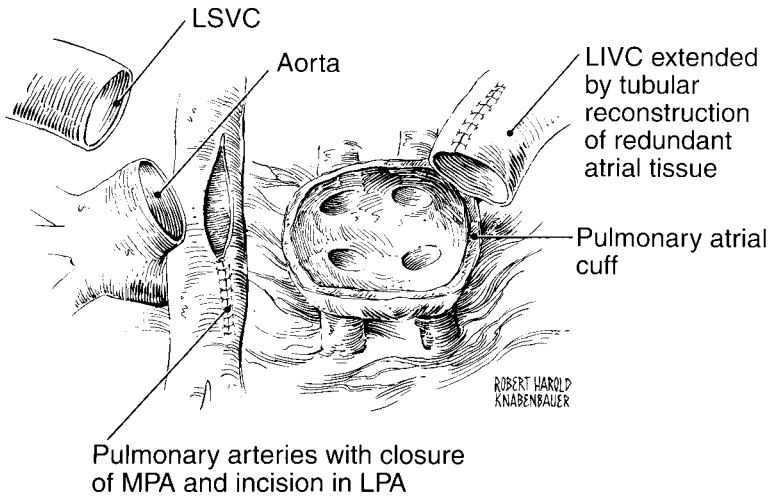

Fig. 2. After cardiectomy, the IVC and attached portion of systemic atrium are configured into a rightward rerouting conduit. The pulmonary artery is opened to the left of the midline and partially oversewn to the right, allowing the anastomotic site to be placed to the left of the aorta. The pulmonary venous atrial cuff lies slightly to the right of midline. *LSVC*, Left superior vena cava; *LIVC*, left inferior vena cava; *MPA*, main pulmonary artery; *LPA*, left pulmonary artery.

vein, which was later used for reconstruction of cephalic venous drainage in the recipient. More or less of the aorta and the pulmonary arterial vessels was obtained with the heart graft depending on the specific recipient requirements. The donor graft was prepared by ligating or oversewing the left pulmonary venous orifices and opening the left atrium vertically and, to some extent, horizontally between the right pulmonary veins (Fig. 1). This

Table I. *Characteristics of 15 pediatric patients with heart transplantation and atrial situs inversus*

Patient no.	*Sex*	*Age at Htx (yr)*	*Weight at Htx (kg)*	*Indications for Htx*	*Collateral conditions*	*CPB (min)*	*HCA* (min)*
1	M	6.64	20.0	Single ventricle; pulmonary stenosis	Asplenia, visceral heterotaxia	122	49
2	F	6.62	14.0	Single ventricle; tricuspid atresia, ASD; pulmonary/subaortic stenosis	Pulmonary hypertension; cardiac arrest before CPB	162	14
3	F	17.71	36.5	Double outlet right ventricle; pulmonary atresia	None	187	25
4	F	6.86	17.7	Double outlet right ventricle; VSD (repaired); aortic stenosis	Visceral heterotaxia; aortic coarctation (repaired)	111	63
5	F	0.04	2.8	Unbalanced AV canal; interrupted aortic arch	Asplenia, visceral heterotaxia	141	65
6	M	14.69	33.3	Double outlet right ventricle; hypoplastic left ventricle; transposition of the great arteries	Visceral heterotaxia	152	45
7	M	15.74	96.0	Idiopathic dilative cardiomyopathy	Status-post VSD closure; Klinefelter's syndrome	177	64
8	F	2.41	10.0	Unbalanced AV canal; TAPVC	Asplenia; failed Fontan	137	24
9	M	6.82	16.8	Single ventricle; pulmonary stenosis	Asplenia	164	53
10	F	0.08	4.0	Unbalanced AV canal; pulmonary atresia	None	117	29
11	F	5.69	17.0	Single ventricle; pulmonary stenosis	None	214	35
12	F	3.68	13.6	Univentricular heart	Asplenia, visceral heterotaxia; failed Fontan; cardiac arrest before CPB	192	46
13	F	0.23	3.7	Unbalanced AV canal; transposition of the great arteries; pulmonary stenosis	Visceral heterotaxia; Ivemark's syndrome	104	32
14	M	0.03	2.8	Single ventricle; transposition of the great arteries; pulmonary atresia; TAPVC	Asplenia, visceral heterotaxia	115	58
15	F	5.63	19.6	Single ventricle	Visceral heterotaxia; failed Fontan	140	67

Htx, Heart transplantation; *CPB,* cardiopulmonary bypass; *HCA,* hypothermic circulatory arrest; *ASD,* atrial septal defect; *VSD,* ventricular septal defect; *AV,* atrioventricular; *TAPVC,* total anomalous pulmonary venous connection.

*Time expressed as a total of several increments of circulatory arrest used to accomplish transplantation.

simple maneuver helps to align the donor's and the recipient's right-sided pulmonary atrium for anastomosis.

Cardiopulmonary bypass was instituted by using a single aortic and atrial cannula. The recipient's body was systemically cooled to 18° to 20° C. Recipient cardiectomy was performed leaving a small pulmonary atrial cuff and abundant systemic atrial tissue in continuity with the left-positioned inferior vena cava (IVC). The left pericardium was widely excised to allow left-sided rotation of the graft, once implanted. The remainder of the procedure was accomplished with the use of low-flow hypothermia. Venous return to the extracorporeal apparatus was accomplished by means of one or more active, flexible pump suckers positioned dependently in the left pleural space or in the pericardial well. Brief, intermittent increments of hypothermic circulatory arrest were used when required for proper exposure. The recipient systemic venous atrial remnant was fashioned into a short rightward directed conduit with a running polypropylene suture, thereby directing IVC venous return toward the right side of the recipient (Fig. 2). Graft implantation was accomplished by the performance of the pulmonary atrial anastomosis first. The IVC of the recipient, lengthened toward the right, was then anastomosed to that of the donor heart. The conduit formed by the donor's SVC and innominate vein was anastomosed to the left-sided SVC of the recipient and positioned in the transverse sinus behind (Fig. 3) the aorta and pulmonary artery. The aortic anastomosis was then performed, followed by removal of the aortic cross-clamp, allowing gentle, initially low-flow, hypothermic graft reperfusion. Systemic rewarming was commenced, and the extracorporeal flow rate and perfusate hematocrit level were gradually increased paralleling the increase in temperature. During the early phase of reperfusion, the recipient's pulmonary artery was opened longitudinally into the left pulmonary artery. The short stump of the main pulmonary artery was closed right to left with a running suture, leaving a left-sided recipient pulmonary

Major postoperative events	*Status*
Mild pancreatitis; chylothorax; need for late SVC venoplasty	Alive
Operative mortality (acute graft failure)	Deceased (operative)
Mild pancreatitis; perioperative seizure	Alive
Chylothorax	Deceased (late); lymphoma
Rejection	Alive
None	Alive
None; late partial SVC obstruction (resolved)	Alive
Perioperative seizure; chylothorax	Alive
None	Alive
None	Alive
None	Alive
Heart block (pacemaker); renal failure (resolved); chylothorax	Deceased (late); rejection
None	Alive
None	Deceased (late); meningitis
Respiratory failure; renal failure (resolved); complete SVC occlusion (resolved)	Alive

arterial orifice for anastomosis with the donor main pulmonary artery (Fig. 2). In infants who require extended aortic arch reconstruction under hypothermic circulatory arrest, the aortic anastomosis was usually accomplished before an SVC connection was performed. This was done to facilitate technical reconstruction of the aortic arch and to enable earlier graft reperfusion. When the aortic reconstruction was accomplished before the cephalic venous connection, the donor SVC–innominate vein conduit was positioned anterior to the great arteries (Fig. 4). All suture lines were accomplished with running polypropylene suture of various sizes. Among the patients in this series, the SVC–innominate vein conduit was placed in the transverse sinus in seven patients and anterior to the aorta and pulmonary artery in six patients. In two instances, the left SVC was ligated, and the donor SVC was anastomosed directly to the recipient's innominate vein. Heart grafts were given a minimum of 60 minutes of extracorporeal reperfusion to assure restoration of functional integrity.

Results

Orthotopic heart transplantation was accomplished successfully in all patients. Median cardiopulmonary bypass time and the total of intermittent serial hypothermic circulatory arrest periods was 149 ± 33 minutes and 44 ± 17 minutes, respectively. Significant perioperative events and late complications are shown in Table I.

Perioperative renal insufficiency requiring peritoneal dialysis developed in two patients, whose renal function normalized before discharge. Postoperative headache prodrome leading to seizure activity was observed in two recipients whose hypertension after transplantation was not well controlled. Intravenous anticonvulsant therapy and more vigorous control of hypertension (and the so-called "posttransplantation high cardiac output state") abolished both the seizures and the headaches. There have been no late neurologic sequelae. Respiratory failure requiring tracheostomy and left diaphragm plication was observed in one of the 15 patients in the present series. The left phrenic nerve was injured during redissection. The condition of patient 1 required late serial balloon venoplasties of a stenotic SVC connection 14 and 17 months after the transplantation. In this particular case, the donor SVC was directly anastomosed to the innominate vein of the recipient, and the left SVC was ligated. Patient 15, with the donor SVC–innominate vein conduit positioned in the transverse sinus beneath the aorta, showed complete obstruction of the SVC 4 years after transplantation. The obstruction produced few symptoms because of a large azygos system that decompressed the SVC. Another recipient (patient 7) experienced the development of a late partial obstruction of SVC drainage, first noted nearly 4 years after transplantation. Late venous obstructions in both patients 7 and 15 related to compression of the venous channel by the great arteries, mainly the aorta. No other significant postoperative cardiac complications (excluding rejection) have occurred among the 11 late survivors.

One hospital death was caused by acute graft failure within 48 hours of the transplantation, which was refractory to extracorporeal circulatory support. Three late deaths were caused by rejection, intracranial lymphoma, and bacterial meningitis. Five-year actuarial survivals after transplantation in patients with situs inversus (79%) are compared in Fig. 5 with those of the 290 patients with atrial situs solitus and complex congenital heart disease or dilated cardiomyopathy.

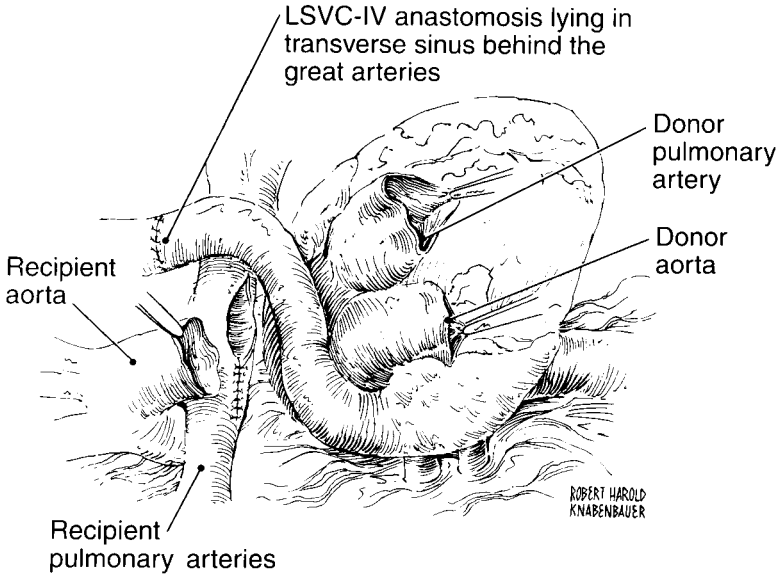

Fig. 3. The conduit formed by the donor's SVC and innominate vein is connected to the left-sided native SVC after being positioned in the transverse sinus behind the great arteries. *LSVC-IV*, Left superior vena cava–innominate vein.

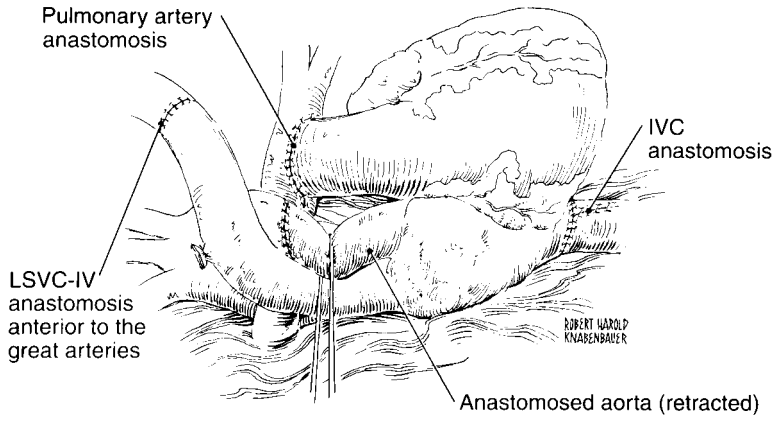

Fig. 4. The conduit formed by the donor's SVC and innominate vein is connected to the left-sided native SVC, in front of the aortic and pulmonary anastomoses. *LSVC-IV*, Left superior vena cava–innominate vein.

Comment

Heart transplantation in infants and children with congenital heart disease frequently represents a technical challenge to the surgeon because of previous palliative procedures, complex structural anomalies,[1] such as atrial malposition, or a combination of both. There have been a few isolated case reports of heart transplantation in the setting of atrial situs inversus, each with a different twist on how to do it. This report of a series of heart transplantation procedures in recipients with situs inversus highlights relatively uniform and simplified technical features.

Doty and coworkers[2] pointed out that some anatomic relations appear to be almost constantly preserved in patients with complex cardiac anomalies and, in particular, in those with situs inversus. The left atrium and main pulmonary artery are midline

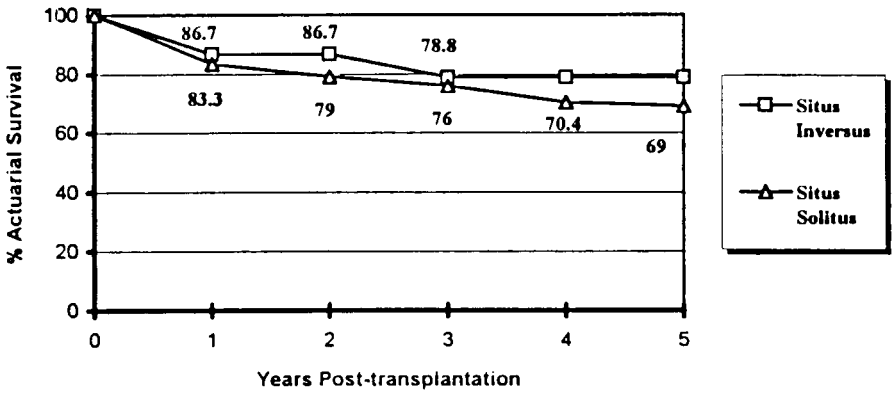

Fig. 5. Five-year actuarial survival curve (including operative mortality rates) in 15 patients with heart transplantation and situs inversus as compared with 290 patients with situs solitus and complex congenital heart disease or dilated cardiomyopathy who underwent transplantation (November 1985 through February 1997).

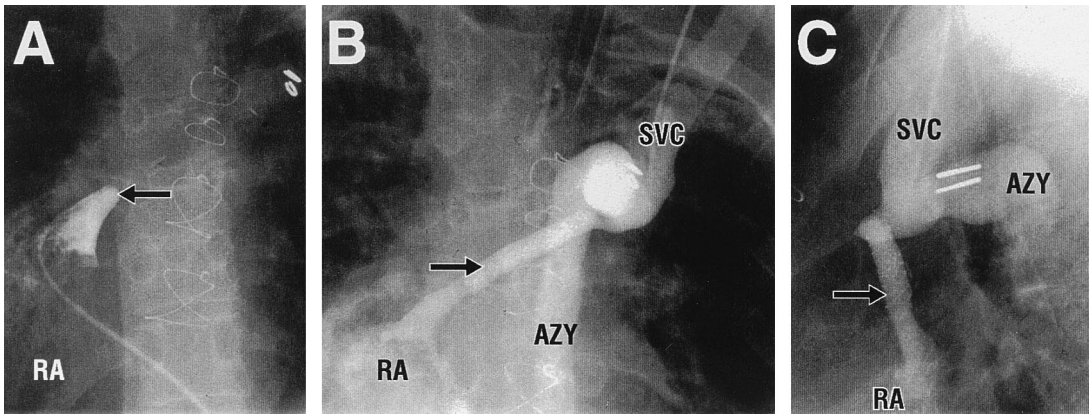

Fig. 6. Cineangiographic appearance of the cephalic venous connection in patient 15. **A**, The catheter in the systemic venous atrium with contrast injection shows complete occlusion of the SVC connection *(arrow)*. *RA*, Right atrium. **B**, Anteroposterior view of the SVC–innominate venous connection after balloon venoplasty and stenting (three overlapping stents) to a diameter of 7 mm. The *arrow* points to the stented donor innominate vein. *AZY*, Azygos. **C,** Lateral view of the stented SVC–innominate venous connection shows flow of contrast into the systemic venous atrium. Stenting of the venous connection was accompanied by a drop in SVC pressure from 13 mm Hg to 11 mm Hg. The dilated azygos *(AZY)* venous system had partially decompressed the SVC. The *arrow* identifies the stented innominate vein.

structures; the aorta is usually to the left of the pulmonary artery as they both exit the pericardium, even in patients with transposition abnormalities. Reconstruction of the mirror-image systemic venous inflow tracts remains the operative challenge in patients with situs inversus, because the left atrium, aorta, and pulmonary artery can usually be anastomosed near the midline. Opening the donor left atrium between the right superior and inferior pulmonary veins, as described earlier, serves the purpose of juxtaposing donor and recipient pulmonary atria near the midline.

Among cases previously reported, transplantation was accomplished by a variety of detailed reconstructive techniques, such as interposed spiral saphenous vein graft,[3] superior and inferior intraatrial baffles,[4, 5] composite cavopericardial graft to right innominate vein and diaphragmatic pericardial tunnel,[2, 6, 7] and separate right and left pulmonary vein cuffs.[8] Use of a Dacron conduit between the right

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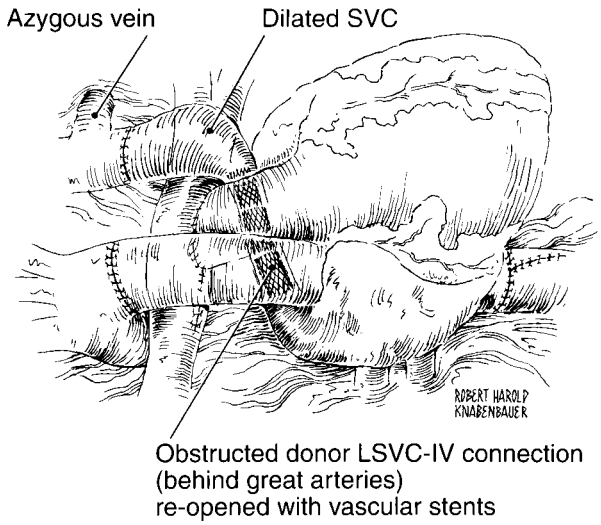

Fig. 7. Artist's depiction of the left superior vena caval–innominate vein *(LSVC-IV)* obstruction managed by interventional stent venoplasty comparable with Fig. 6, **B.**

atrium and left SVC[9] and counterclockwise rotation with the left-sided IVC anastomosis[10] have also been used to restore continuity of systemic venous return. The use of devascularized autologous pericardium for rerouting purposes in infants may lead to late venous stenosis. In addition, prosthetic material used in infants and children has no growth potential and may become a site for infection, when compared with autologous or donor tissue. The technique presented in this report is simple and relatively free of late complications. Mean cardiopulmonary bypass and circulatory arrest times compared favorably with those of infants and children with situs solitus undergoing heart transplantation (98 ± 37 minutes and 48 ± 16 minutes, respectively, in the latter group).

Parry and coworkers[3] have raised the question of left phrenic nerve compression secondary to leftward relocation of the graft and proposed, as alternatives, anterior deflection of the phrenic nerve or creation of a "pericardiopleural cradle" by suturing the left pericardial border to the pleurosternal reflection. Permitting the left phrenic nerve to lie on the hilum of the lung under the newly implanted heart graft has not resulted in any diaphragmatic paresis or respiratory sequelae among survivors in the present series.

The method of venous connection, and in particular the course of the SVC-innominate conduit (anterior to the aorta or in the transverse sinus), remains open for debate. Patient 1 had recurrent stricture of the SVC after direct anastomosis of the SVC to the recipient's innominate vein, with ligation of the native left SVC. A larger original anastomosis may have prevented this partial sutureline obstruction. Patients 7 and 15 had delayed occlusion, believed to be compressive in nature, of the posteriorly positioned (transverse sinus) donor SVC–innominate venous conduit. None of the patients with left SVC connections established anteriorly have experienced systemic venous obstruction. Because placement of the cephalic venous drainage conduit is largely determined by relatively fixed anatomic considerations, no clear recommendation based on outcome can be made. However, experience suggests that when the cephalic venous drainage conduit is to be draped over a large ascending aorta, shortening the ascending aortic reconnection may prove beneficial by prevention of stretching and flattening of the venous pathway. By contrast, when the SVC connection is established behind the great arteries, it may prove beneficial to procure enough ascending aorta (along with the cardiac graft) with which to slightly lengthen its course and relieve posterior compression of the venous conduit.

Various methods of the assessment of long-term patency of venous reconstruction, including angiography and magnetic resonance imaging,[4, 7] have been used. Color-flow Doppler imaging is a useful, noninvasive modality to assess patency of venous connections. The central venous system may be visualized during right-sided catheterizations for endomyocardial biopsy. Access through the IVC anastomosis or, when femoral venous access is unavailable, through the SVC–innominate venous conduit has not been particularly difficult in most of the patients in this series. The condition of each patient with late cephalic venous obstruction has been successfully managed with interventional techniques applied in the cardiac catheterization laboratory. The anastomotic stricture in patient 1 has yielded to serial balloon venoplasties. The compressive obstructions in patients 7 and 15 have been relieved by a combination of venoplasty and placement of endovascular stents (Figs. 6 and 7). Natural decompression of the obstructed SVC by the azygos system reduced the SVC pressure from a high of 26 mm Hg to 13 mm Hg over a 12-month period. Angioplasty and initial stenting to a diameter of 7 mm has resulted in a further reduction in SVC pressure to 11 mm Hg. Additional dilation of the stents is planned. None of the 14 early or the 11 late

survivors of heart transplantation in this series has experienced symptomatic SVC syndrome, although signs of cephalic venous hypertension were apparent (i.e., exaggerated venous collateral pattern on the upper torso).

Conclusions

Orthotopic heart transplantation has been safely accomplished with relative ease among infants and children with situs inversus. The short- and long-term morbidity and mortality rates are comparable with patients with situs solitus. Rerouting of systemic venous drainage by simple techniques, such as those described, seems preferable to more complex reconstructive methods.

We thank Drs. Mark Reller and Grant Burch, pediatric cardiologists at the University of Oregon Health Sciences Center, Doernbecher Children's Hospital, for their care of patient 15. Their skillful intervention reestablished cephalic venous drainage through the donor SVC–innominate vein in this child. They provided the cineangiography (Fig. 6).

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